

**REMARKS/ARGUMENTS**

Claims 48-59 and 63-75 have been examined. With entry of this amendment, claims 48-58 and 63-75 are pending in the above-identified application. Claims 55-58 are withdrawn from consideration by the Examiner as being drawn to a non-elected invention and have been cancelled by this response. Claim 59 has been canceled in order to further expedite prosecution of the instant application. Further, claims 48, 49, 51-53, 63-66, 71, 72, and 74 have been amended as described in detail below. The specification has also been amended to delete any browser-executable code. Applicants expressly reserve the right to prosecute any subject matter canceled by the amendments set forth herein in a related, co-pending application. No new matter is believed to be added by these amendments.

Claims 52, 53, and 72 are amended to set forth specific embodiments of the present invention with greater clarity by reciting, with more particular reference to "a recombinant  $\alpha 1 \rightarrow 2$  fucosyltransferase," the amino acid or nucleotide sequence identifier already recited in the respective claims with regard to recombinant cells. Claim 53 has been amended to correct a typographical error by substituting "the nucleotide sequence ..." for "a nucleotide sequence ...." Claim 74 has also amended to correct a typographical error by deleting "7" and inserting "9" for the recited SEQ ID NO.; with this amendment, claim 74, which is dependent on claim 71, now recites the correct nucleotide sequence encoding the amino acid sequence recited in claim 71.

**Rejections Under 35 U.S.C. § 112, Second Paragraph:**

Claims 53, 59, and 74 stand rejected under 35 U.S.C. § 112, second paragraph, the Examiner believing the claims to be indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claim 59 stands rejected as depending from a canceled claim. Further, the Examiner believes that the phrase "isolated or purified recombinant ..." is indefinite because it is not clear to the Examiner

"whether applicants are claiming an isolated and purified enzyme or a recombinant enzyme."  
Also, claim 74, depending from claim 71 (which recites the amino acid sequence SEQ ID NO:10) stands rejected for the recitation of SEQ ID NO: 7, which encodes the amino acid sequence of SEQ ID NO: 8.

With respect to claims 59 and 74, the instant rejection is obviated by Applicants' cancellation of claim 59 and amendment of claim 74 as set forth above.

With respect to claim 53, Applicants respectfully traverse the instant rejection. The determination of whether a claim is definite depends on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the specification. *See North Am. Vaccine, Inc. v. American Cyanamid Co.*, 28 USPQ2d 1333, 1339 (Fed. Cir. 1993). The skilled artisan reading claim 53 in light of the specification would understand the term "isolated or purified recombinant" enzyme to mean a recombinant enzyme that is isolated or purified from a recombinant cell, as opposed to isolated or purified from natural sources. (*See, e.g.*, page 24, line 30, bridging to page 25, line 16, which describes, *inter alia*, the identification of a recombinant protein produced by a recombinant cell, its subsequent isolation or purification, and the isolation or purification from natural sources.) Thus, Applicants believe that claim 53 is definite.

To further expedite prosecution, however, Applicants have amended claim 53 to delete the term "isolated or purified." Because a "recombinant" enzyme can be, for example, isolated or purified or contained within a recombinant cell or recombinant cell lysate, and because the skilled artisan reading the amended claim would understand this meaning in light of the specification (see above), Applicants believe that this amendment does not narrow the scope of claim 53.

In view of the above remarks and amendments, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claim 53, 59, and 74 under 35 U.S.C. § 112, second paragraph.

Rejections Under 35 U.S.C. § 112, First Paragraph:

Claims 52, 72, and 73 stand rejected under 35 U.S.C. § 112, first paragraph, the Examiner believing that the specification, while enabling for a method for synthesizing a fucosylated molecule or a fucosyl-GM1 using an enzyme having  $\alpha$  1,2-fucosyltransferase (FT) activity and comprising the amino acid sequence set forth in SEQ ID NO:8 or 10, "does not reasonably provide enablement for such a method using any recombinant  $\alpha$  1,2-fucosyltransferase."

While Applicants disagree with the Examiner's characterization of the specification with regard to enablement of recombinant  $\alpha$  1,2-fucosyltransferases other than those comprising the amino acid sequence set forth in SEQ ID NO:8 or 10, Applicants believe the instant rejection to be obviated by the amendments to claims 52, 72, and 73 as set forth above. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 52, 72, and 73 for alleged lack of enablement under 35 U.S.C. § 112, first paragraph.

Claims 52, 53, and 72 stand rejected under 35 U.S.C. § 112, first paragraph, the Examiner believing these claims to contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

While Applicants disagree with the Examiner's characterization of the specification with regard to written description of recombinant  $\alpha$  1,2-fucosyltransferases other than those comprising the amino acid sequence set forth in SEQ ID NO:8 or 10, Applicants believe the instant rejection to be obviated by the amendments to claims 52, 53, and 72 as set forth above. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 52, 72, and 73 for alleged lack of written description under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 102(b):

Claims 48-51, 53, 54, 63-71, and 74 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Holmes *et al.* (*J. Biol. Chem.* 258:3706-3713, 1983). The Examiner states that the enzyme isolated from Holmes *et al.* has "identical properties" as that used in the methods of the present invention, and, based on principles of inherency, takes the position that the enzyme used in the claimed methods and that disclosed in the reference is "one and the same," *i.e.*, that "the amino acid sequence of the enzyme in the reference is that of either SEQ ID NO:8 or 10."

Applicants respectfully traverse the instant rejection. For a reference to inherently disclose a claim limitation, the recited limitation must be "*necessarily present*" in the reference. *Crown Operations International Ltd. v. Solutia Inc.*, 289 F.3d 1367, 62 USPQ2d 1917, 1923 (Fed. Cir. 2002) (emphasis added). "Inherency ... may not be established by probabilities or possibilities." *Continental Can. Co. USA, Inc. v. Monsanto Co.*, 948 F.2d. 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). In the present case, Applicants believe that the Examiner has not set forth sufficient facts to support a *prima facie* case for inherency. Holmes *et al.* disclose at most a crude homogenate and Golgi membrane preparation that comprise a  $\alpha$ -L-fucosyltransferase activity. It can not be concluded from the teachings of Holmes *et al.* that the activity detected resulted from a single enzyme, multiple enzymes, or whether the activity resulted from one or more isoforms of an enzyme. Natural isoforms for a given protein are commonly found in biological systems, including within the same species. See, for example, page 2, line 24 through page 3, line 5 of the specification. Therefore, a skilled artisan would not presume that the  $\alpha$  1,2-fucosyltransferase described in Holmes *et al.* has the identical amino acid sequence set forth in either SEQ ID NO:8 or 10. Accordingly, Applicants submit that the amino acid sequence set forth in SEQ ID NO:8 or 10 is not necessarily present, and thus not inherent, in the  $\alpha$  1,2-fucosyltransferase activity described in Holmes *et al.*

However, to further expedite prosecution of the instant application, Applicants have amended independent claims 48, 49, 51, 63-66, and 71 by deleting the phrase "isolated or purified" and inserting the term "recombinant" in reference to an  $\alpha 1 \rightarrow 2$  fucosyltransferase. Support for these amendments are found throughout the specification (for example, page 24, line 21, bridging to page 25, line 16) and in the original claims. Applicants note that claim 53 already recites "recombinant  $\alpha 1 \rightarrow 2$  fucosyltransferase" in view of the amendment set forth above with respect to Applicants' response under 35 U.S.C. §112, second paragraph. Also, as noted above, a skilled artisan reading the specification would understand a recombinant enzyme can include as a particular embodiment a recombinant enzyme isolated or purified from a recombinant cell.

In view of the above remarks and amendments, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 48-51, 53, 54, 63-71, and 74 as allegedly anticipated by Holmes *et al.* under 35 U.S.C. § 102(b).

Rejections Under 35 U.S.C. § 103:

Claims 52, 72-73, and 75 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Holmes *et al.* as applied to claims 48-51, 53, 54, 63-71, and 74, and further in view of "the common knowledge in the art of protein purification and molecular cloning techniques." The Examiner believes that it would have been obvious to those skilled in the art to "purify the enzyme [described in Holmes *et al.*] further ..., obtain the amino acid sequence and obtain a cDNA clone and arrive at a recombinant enzyme by using the common knowledge available in the art of molecular biology ...."

Applicants respectfully traverse the instant rejection. Applicants disagree with the Examiner's basis for the rejection and believe that the Examiner has not established a proper *prima facie* case of obviousness. A *prima facie* case of obviousness under 35 U.S.C. § 103 requires, *inter alia*, that the prior art teach or suggest *all* the claim limitations. MPEP §2143 at

2100-125. In the present case, the Examiner has not established a teaching or suggestion in the prior art of a "recombinant  $\alpha 1 \rightarrow 2$  fucosyltransferase" as recited in the claims, since neither Holmes *et al.* nor the common knowledge in the art contain any teaching or suggestion of a DNA molecule encoding the respective  $\alpha 1 \rightarrow 2$  fucosyltransferase enzyme.

First, Applicants submit that a cDNA encoding an  $\alpha 1 \rightarrow 2$  fucosyltransferase having SEQ ID NO:8 or 10 was not known or obvious as of the effective filing date of the instant application. It is well-established that a DNA molecule encoding a protein is not rendered obvious by general knowledge of methods for obtaining the DNA, even where the protein is known in the art. *In re Deuel*, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995); *In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993). As the Federal Circuit has stated, "in the absence of other prior art" that suggests specific DNA molecules, "the existence of a general method of isolating cDNA or DNA molecules is essentially irrelevant to the question [of] whether the specific molecules themselves would have been obvious." *In re Deuel*, 34 USPQ2d at 1215 (reaffirming *In re Bell*, 26 USPQ2d 1529).

Second, Applicants believe that a method of preparative synthesis of a molecule comprising  $\text{Fu}\alpha 1 \rightarrow 2\text{Gal}\beta 1 \rightarrow 3\text{GalNac}$  by contacting a *recombinant*  $\alpha 1 \rightarrow 2$  fucosyltransferase, produced by methods using a DNA encoding it, cannot be obvious where a DNA molecule encoding the  $\alpha 1 \rightarrow 2$  fucosyltransferase is not known or obvious. Where (a) one or more starting materials are not known or obvious and (b) a general process *can* be modified by using the unknown or nonobvious starting material to yield a specific process for producing a specific product, the specific process as well as the specific product are not rendered obvious by knowledge in the art of the general process. *See, e.g., In re Ochiai*, 37 USPQ2d 1127, 1131 (Fed. Cir. 1995). Thus, Applicants respectfully submit that because the DNA encoding the recited  $\alpha 1 \rightarrow 2$  fucosyltransferase was not known or obvious as of the effective filing date, as set forth above, preparative methods as recited in claims 52, 72-73, and 75 are also not obvious.

Further, Holmes *et al.* is not an appropriate reference to support the obviousness rejection asserted by the Examiner of the pending claims because the reference does not disclose

an amino acid sequence for the isolated enzyme. Even assuming, *arguendo*, that the amino acid sequence as depicted in SEQ ID NO:8 or 10 is an inherent characteristic of the  $\alpha 1 \rightarrow 2$  fucosyltransferase in Holmes *et al.*, the test for inherency is distinct from that for obviousness, *e.g.*, *In re Spormann*, 150 USPQ 449, 452 (CCPA 1966). Inherency is not obviousness, since "[t]hat which may be inherent is not necessarily known," and "obviousness cannot be predicated on what is unknown." *Id.* In this case, neither the amino acid sequence set forth in SEQ ID NO:8 or 10 nor a nucleotide sequence of a DNA encoding it were known at the time of filing of the instant application. Accordingly, Applicants believe that a rejection of claims 52, 72-73, and 75 under 35 U.S.C. § 103 cannot be predicated on alleged inherent disclosure of an amino acid sequence as set forth in SEQ ID NO:8 or 10.

Therefore, Applicants believe that the methods recited in claims 52, 72-73, and 75 are nonobvious in view of Holmes *et al.* and the general knowledge in the art and, further, that the Examiner has not established a *prima facie* case under 35 U.S.C. § 103. In view of the above remarks and amendments, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 52, 72-73, and 75 under 35 U.S.C. § 103(a).

35 U.S.C § 101 Double Patenting:

Claims 48-54 stand rejected under 35 U.S.C § 101 for statutory type double patenting as conflicting with claims 48-54 of Application No. 09/999,672.

Applicants respectfully refer the Examiner to the Applicants' Communication of September 29, 2003, transmitting a copy of pages 2-4 of a preliminary amendment filed May 23, 2003 in Application No. 09/999,672 (the '672 application; issued as U.S. Patent 6,656,714 (the '714 patent), on December 2, 2003). As stated in the Communication, the preliminary amendment of May 23, 2003 comprises the claims allowed in the '672 application and now issued as the '714 patent. Applicants further note that the claims which have issued in the '714 patent do not conflict with claims 48-54 of the present case under 35 U.S.C. § 101 because the claims of the '714 patent and present application belong to separate groups of the restriction

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Appl. No. 10/040,863  
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requirement in the parent case. As such the PTO has decided that the respective subject matter comprise separate inventions. Thus, claims 48-54 cannot be rejected under 35 U.S.C. § 101 for statutory type double patenting. Applicants therefore respectfully request the Examiner to reconsider and withdraw the rejection of claims 48-54 for statutory type double patenting under 35 U.S.C § 101.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

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